

|  |  |  |  |                                      |
|--|--|--|--|--------------------------------------|
| Substitute Form PTO-1449<br>(Modified)<br><br><b>Information Disclosure Statement<br/>by Applicant</b><br>(Use several sheets if necessary)<br><br>(37 CFR §1.98(b)) | U.S. Department of Commerce<br>Patent and Trademark Office |  | Attorney's Docket No.<br><b>20750-050US1</b> | Application No.<br><b>10/593,847</b> |
|  | Applicant<br><b>John Robert Fritch, et al.</b>             |  |  |                                      |
|  | Filing Date<br><b>August 2, 2007</b>                       |  | Group Art Unit                               |                                      |
|  |  |  |  |                                      |

**U.S. Patent Documents**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Patentee              | Class | Subclass | Filing Date If Appropriate |
|------------------|-----------|-----------------|------------------|-----------------------|-------|----------|----------------------------|
|                  | A1        | US 4099012      | 7/04/78          | Gshwend               |       |          |                            |
|                  | A2        | US 4405644      | 9/20/83          | Kabbe et al.          |       |          |                            |
|                  | A3        | US 4409231      | 10/11/83         | Stenzel et al.        |       |          |                            |
|                  | A4        | US 4985352      | 1/15/91          | Julius et al.         |       |          |                            |
|                  | A5        | US 5077409      | 12/31/91         | Wissner               |       |          |                            |
|                  | A6        | US 5128351      | 7/07/92          | Wissner               |       |          |                            |
|                  | A7        | US 5523280      | 6/04/96          | Chenc et al.          |       |          |                            |
|                  | A8        | US 5661024      | 8/26/97          | Kao et al.            |       |          |                            |
|                  | A9        | US 5886044      | 3/23/99          | Widdowson et al.      |       |          |                            |
|                  | A10       | US 5905080      | 5/18/99          | Duckworth et al.      |       |          |                            |
|                  | A11       | US 5945382      | 8/31/99          | Cantegril et al.      |       |          |                            |
|                  | A12       | US 5990133      | 11/23/99         | Gaster et al.         |       |          |                            |
|                  | A13       | US 6005008      | 12/21/99         | Widdowson et al.      |       |          |                            |
|                  | A14       | US 6028085      | 2/22/00          | Bromidge              |       |          |                            |
|                  | A15       | US 6054472      | 4/25/00          | Armistead et al.      |       |          |                            |
|                  | A16       | US 6107324      | 08/ /02          | Behan et al.          |       |          |                            |
|                  | A17       | US 6140509      | 10/31/00         | Behan et al.          |       |          |                            |
|                  | A18       | US 6271261      | 8/07/01          | Widdowson             |       |          |                            |
|                  | A19       | US 2002/0025965 | 2/28/02          | Lavielle et al.       |       |          |                            |
|                  | A20       | US 6417393      | 7/09/02          | Christophersen et al. |       |          |                            |
|                  | A21       | US 6479480      | 11/12/02         | Moyes et al.          |       |          |                            |
|                  | A22       | US 6479519      | 11/12/02         | Astles et al.         |       |          |                            |
|                  | A23       | US 6541209      | 4/01/03          | Behan et al.          |       |          |                            |
|                  | A24       | US 6706749      | 3/16/04          | Dahl et al.           |       |          |                            |
|                  | A25       | US 2004/0102636 | 5/27/04          | Miller et al.         |       |          |                            |
|                  | A26       | US 6784183      | 8/31/04          | Lavielle et al.       |       |          |                            |
|                  | A27       | US 2005/0080124 | 04/14/2005       | Tecgarden et al.      |       |          |                            |

|  |                 |
|--|-----------------|
| Examiner Signature   | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |

|   |  |   |                               |
|---|--|---|-------------------------------|
| Substitute Form PTO-1449<br>(Modified)  | U.S. Department of Commerce<br>Patent and Trademark Office | Attorney's Docket No.<br>20750-050US1   | Application No.<br>10/593,847 |
| <b>Information Disclosure Statement<br/>by Applicant</b><br>(Use several sheets if necessary) |  | Applicant<br>John Robert Fritch, et al. |                               |
|   |  | Filing Date<br>August 2, 2007           | Group Art Unit                |

(37 CFR §1.98(b))

### Foreign Patent Documents or Published Foreign Patent Applications

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation |    |
|------------------|-----------|-----------------|------------------|--------------------------|-------|----------|-------------|----|
|                  |           |                 |                  |                          |       |          | Yes         | No |
|                  | A28       | WO 96/02138     | 2/01/96          | WIPO                     |       |          |             |    |
|                  | A29       | WO 96/10559     | 4/11/96          | WIPO                     |       |          |             |    |
|                  | A30       | WO 97/03967     | 2/06/97          | WIPO                     |       |          |             |    |
|                  | A31       | WO 97/45111     | 12/04/97         | WIPO                     |       |          |             |    |
|                  | A32       | WO 98/24785     | 6/11/98          | WIPO                     |       |          |             |    |
|                  | A33       | WO 99/06354     | 2/11/99          | WIPO                     |       |          |             |    |
|                  | A34       | WO 99/32436     | 7/01/99          | WIPO                     |       |          |             |    |
|                  | A35       | WO 99/32463     | 7/01/99          | WIPO                     |       |          |             |    |
|                  | A36       | WO 99/52927     | 10/21/99         | WIPO                     |       |          |             |    |
|                  | A37       | WO 00/57877 A1  | 10/05/00         | WIPO                     |       |          |             |    |
|                  | A38       | WO 2000/064866  | 11/02/00         | WIPO                     |       |          |             |    |
|                  | A39       | WO 2001/021160  | 3/29/01          | WIPO                     |       |          |             |    |
|                  | A40       | WO 01/29008     | 4/26/01          | WIPO                     |       |          |             |    |
|                  | A41       | EP 1108720 A1   | 6/20/01          | Europe                   |       |          |             |    |
|                  | A42       | WO 2002/039987  | 5/23/02          | WIPO                     |       |          |             |    |
|                  | A43       | WO 02/076464    | 10/03/02         | WIPO                     |       |          |             |    |
|                  | A44       | WO 03/062206    | 7/31/03          | WIPO                     |       |          |             |    |
|                  | A45       | WO 04/028450    | 4/08/04          | WIPO                     |       |          |             |    |
|                  | A46       | WO 04/058722    | 7/15/04          | WIPO                     |       |          |             |    |
|                  | A47       | WO 2004/071426  | 8/26/04          | WIPO                     |       |          |             |    |
|                  | A48       | WO 2004/085433  | 10/07/04         | WIPO                     |       |          |             |    |
|                  | A49       | WO 04/096771    | 11/11/04         | WIPO                     |       |          |             |    |
|                  | A50       | WO 2006/018662  | 2/23/06          | WIPO                     |       |          |             |    |
|                  | A51       | WO 2006/049941  | 5/11/06          | WIPO                     |       |          |             |    |
|                  | A52       | WO 2006/060654  | 6/08/06          | WIPO                     |       |          |             |    |
|                  | A53       | WO 2006/076592  | 7/20/06          | WIPO                     |       |          |             |    |
|                  | A54       | WO 2006/089871  | 8/31/06          | WIPO                     |       |          |             |    |

|  |                 |
|--|-----------------|
| Examiner Signature   | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |

|   |  |  |                               |
|---|--|--|-------------------------------|
| Substitute Form PTO-1449<br>(Modified)  | U.S. Department of Commerce<br>Patent and Trademark Office | Attorney's Docket No.<br>20750-050US1          | Application No.<br>10/593,847 |
| <b>Information Disclosure Statement<br/>by Applicant</b><br>(Use several sheets if necessary) |  | Applicant<br><b>John Robert Fritch, et al.</b> |                               |
|   |  | Filing Date<br><b>August 2, 2007</b>           | Group Art Unit                |

(37 CFR §1.98(b))

**Foreign Patent Documents or Published Foreign Patent Applications**

| Examiner Initial | Desig. ID | Document Number | Publication Date | Country or Patent Office | Class | Subclass | Translation |    |
|------------------|-----------|-----------------|------------------|--------------------------|-------|----------|-------------|----|
|                  |           |                 |                  |                          |       |          | Yes         | No |
|                  | A55       | WO2006/081335   | 8/3/06           | WIPO                     |       |          |             |    |
|                  | A56       | EP 1734039      | 12/20/06         | Europe                   |       |          |             |    |

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document   |
|------------------|-----------|--|
|                  | A57       | Andrzejewska-Buczko et al., "Serotonin in diabetic retinopathy", Klin Oczna 1996 Feb; 98(2):101-4 (abstract only)  |
|                  | A58       | Berge et al., "Pharmaceutical salts", J. of Pharmaceutical Sciences (1977) 66(1):1-19  |
|                  | A59       | Cameron et al., "The effects of 5-hydroxytryptamine 5-HT <sub>2</sub> receptor antagonists on nerve conduction velocity and endoneurial perfusion in diabetic rats", Naunyn Schmiedeberg's Arch Pharmacol, 2003 Jun; 367(6):607-14   |
|                  | A60       | Casey et al., "Constitutively active mutant 5HT <sub>2A</sub> serotonin receptors: inverse agonist activity of classical 5HT <sub>2A</sub> antagonists", Society for Neuroscience Abstracts, Vol. 22, p. 699.10  |
|                  | A61       | Cazzola et al., "5-HT modifiers as a potential treatment of asthma", TIPS, 2000, Vol. 21, p.13   |
|                  | A62       | Chang et al., "Mechanism of the ocular hypotensive action of ketanserine", J Ocul Pharmacol., 1985 Summer; 1(2):137-47   |
|                  | A63       | Cohen-Mansfield et al., "Agitated behaviors in the elderly. I. A conceptual review", J. Am. Geriatr. Soc., 1986 Oct; 34(10):711-21   |
|                  | A64       | Collier et al., "Radiosynthesis and in-vivo evaluation of the pseudopeptide $\delta$ -opioid antagonist [ <sup>125</sup> I]-ITIPP(p)", J. Labeled Compd. Radiopharm., 1999, Vol. 42, pp. S264-S266   |
|                  | A65       | Collins, et al., "N-Phenylamidines as Selective Inhibitors of Human Neuronal Nitric Oxide Synthase: Structure-Activity Studies and Demonstration of in Vivo Activity", <i>Journal of Medicinal Chemistry, American Chemical Society</i> , 41, no. 15, pp. 2858-2871, 1998; XP0022144154. |
|                  | A66       | De Bie et al., "Modulation of airway hyperresponsiveness and eosinophilia by selective histamine and 5-HT receptor antagonists in a mouse model of allergic asthma", British Journal of Pharmacology, 1998, Vol. 124:857-864   |
|                  | A67       | Greene et al., <i>Protecting Groups in Organic Synthesis</i> , 3 <sup>rd</sup> Edition, 1999 (Wiley)*  |
|                  | A68       | Grunder et al., "Time course of 5-HT <sub>2A</sub> receptor occupancy in the human brain after a single oral dose of the putative antipsychotic drug MDL 100,907 measured by positron emission tomography, Neuropsychopharmacology, 1997 Sep; 17(3):175-85                               |
|                  | A69       | Herrick-Davis et al., "Activating mutations of the serotonin 5-HT <sub>2C</sub> receptor", J. Neurochem., 1997 Sep; 69(3):1138-44  |
|                  | A70       | Herrick-Davis et al., "Constitutively active 5HT <sub>2C</sub> serotonin receptor created by site-directed mutagenesis", Society for Neuroscience Abstracts, Vol. 22, p. 699.18  |
|                  | A71       | Higuchi et al., "Pro-drugs and Novel Delivery Systems", Vol. 14 of the ACS Symposium Series; and in <i>Bio-reversible Carriers in Drug Design</i> , ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987*   |

|  |                 |
|--|-----------------|
| Examiner Signature   | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |

|  |  |  |                                      |
|--|--|--|--------------------------------------|
| Substitute Form PTO-1449<br>(Modified) | U.S. Department of Commerce<br>Patent and Trademark Office | Attorney's Docket No.<br><b>20750-050US1</b>   | Application No.<br><b>10/593,847</b> |
|  |  | Applicant<br><b>John Robert Fritch, et al.</b> |                                      |
|  |  | Filing Date<br><b>August 2, 2007</b>           | Group Art Unit                       |

(37 CFR §1.98(b))

**Other Documents (include Author, Title, Date, and Place of Publication)**

| Examiner Initial | Desig. ID | Document   |
|------------------|-----------|--|
|                  | A72       | Katz et al., "Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. Risperidone Study Group", J. Clin. Psychiatry, 1999 Feb; 60(2):107-15                                    |
|                  | A73       | Koss et al., "Assessing patterns of agitation in Alzheimer's disease patients with the Cohen-Mansfield Agitation Inventory. The Alzheimer's Disease Cooperative Study", Alzheimer Dis Assoc Disord. 1997; 11 Suppl 2:S45-50.                                       |
|                  | A74       | Landolt et al., "Serotonin-2 receptors and human sleep: effect of a selective antagonist on EEG power spectra", Neuropsychopharmacology, 1999 Sep; 21(3):455-66  |
|                  | A75       | Le Bas et al., "Radioiodinated analogs of EP 00652218 for the exploration of the tachykinin NK1 receptor by spect", J. Labeled Compd. Radiopharm., 2001, Vol 44:S280-S282  |
|                  | A76       | Mastropasqua et al., "Ocular hypotensive effect of ketanserin in patients with primary open angle glaucoma", Acta Ophthalmol Scand Suppl., 1997 (224):24-5   |
|                  | A77       | National Institutes of Health, National Heart, Lung and Blood Institute, "Insomnia" (October 1995) pp. 1-4.  |
|                  | A78       | Pietraszek et al., "Blood serotonergic mechanisms in type 2 (non-insulin-dependent) diabetes mellitus", Thromb Res., 1992 Jun 15; 66(6):765-74   |
|                  | A79       | Prosser et al., "Selective serotonin 5-HT <sub>2A</sub> inverse agonists promote sleep consolidation in male Wistar rats during the normal inactive phase", #29, Arena Pharmaceuticals, Inc., APSS Meeting (June 2004) 1 page.                                     |
|                  | A80       | Remington, The Science and Practice of Pharmacy, 20 <sup>th</sup> Edition, 2000 (Lippincott Williams & Wilkins)*   |
|                  | A81       | Satomura et al., "Sarpogrelate, a specific 5HT <sub>2</sub> -receptor antagonist, improves the coronary microcirculation in coronary artery disease", Clin. Cardiol. 2002 Jan; 25(1):28-32   |
|                  | A82       | Sharpley et al., "Slow wave sleep in humans: role of 5-HT <sub>2A</sub> and 5-HT <sub>2C</sub> receptors", Neuropharmacology, 1994 Mar-Apr; 33(3-4):467-71   |
|                  | A83       | Smith et al., "Test-retest variability of serotonin 5-HT <sub>2A</sub> receptor binding measured with positron emission tomography and [18F]altanserin in the human brain, Synapse, 1998 Dec; 30(4):380-92   |
|                  | A84       | Staley et al., "Comparison of [(18F)]altanserin and [(18F)]durtetrolaltanserin for PET imaging of serotonin (2A) receptors in baboon brain: pharmacological studies, Nucl Med Biol, 2001 Apr; 28(3):271-9  |
|                  | A85       | Strah-Pleyne et al., "Discovery and SAR of novel 5-HT <sub>2A</sub> inverse-agonists", 227 ACS National Meeting, MEDI 270, Arena Pharmaceuticals, Inc. (March 2004), 1 page.   |
|                  | A86       | Street et al., "Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double-blind, randomized, placebo-controlled trial. The HGEU Study Group", Arch Gen Psychiatry, 2000 Oct; 57(10):968-76 |
|                  | A87       | Takahashi et al., "Sarpogrelate hydrochloride, a serotonin 2A receptor antagonist, reduces albuminuria in diabetic patients with early-stage diabetic nephropathy", Diabetes Res Clin Pract. 2002 Nov; 58(2):123-9   |
|                  | A88       | Takenaka et al., "The effect of anplag (sarpogrelate HCl), novel selective 5-HT <sub>2</sub> antagonist on intraocular pressure in glaucoma patients", Invest Ophthalmol Vis Sci, 36(4):S724 (3390-377)  |
|                  | A89       | Talvik-Lofli et al., "High 5HT <sub>2A</sub> receptor occupancy in M100907-treated schizophrenic patients", Psychopharmacology (2000) 148:400-403  |

|  |                 |
|--|-----------------|
| Examiner Signature   | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |

|   |  |  |                                      |
|---|--|--|--------------------------------------|
| Substitute Form PTO-1449<br>(Modified)  | U.S. Department of Commerce<br>Patent and Trademark Office | Attorney's Docket No.<br><b>20750-050US1</b>   | Application No.<br><b>10/593,847</b> |
| <b>Information Disclosure Statement<br/>by Applicant</b><br>(Use several sheets if necessary) |  | Applicant<br><b>John Robert Fritch, et al.</b> |                                      |
|   |  | Filing Date<br><b>August 2, 2007</b>           | Group Art Unit                       |
| (37 CFR §1.98(b))   |  |  |                                      |

| Other Documents (include Author, Title, Date, and Place of Publication) |           |   |
|---|-----------|---|
| Examiner Initial  | Desig. ID | Document  |
|   | A90       | The International Classification of Sleep Disorders, Revised Diagnostic and Coding Manual, American Academy of Sleep Medicine (2001) pp. 1-336 (also includes table of contents and glossary)                       |
|   | A91       | Topliss, John G., "A Manual Method for Applying the Hansch Approach to Drug Design", <i>Journal of Medicinal Chemistry</i> , Vol. 20, No. 4, pp. 463-469, 1997.   |
|   | A92       | Wilson et al., "LY53857, a 5HT <sub>2</sub> Receptor Antagonist, Delays Occlusion and Inhibits Platelet Aggregation in a Rabbit Model of Carotid Artery Occlusion", <i>Thromb Haemost.</i> 1991 Sep 2; 66(3):355-60 |
|   | A93       | Winokur et al., "Acute effects of mirtazapine on sleep continuity and sleep architecture in depressed patients: a pilot study", <i>Biol Psychiatry</i> , 2000 Jul 1; 48(1):75-8                                     |
|   | A94       | Zhu et al., "Synthesis and mode of action of [ <sup>125</sup> I]- and <sup>3</sup> H-labeled Thieno -2,3-c[pyridine antagonists of cell adhesion molecule expression", <i>J. Org. Chem.</i> , (200) 67:943-8        |
|   | A95       | Copy of International Search Report dated November 8, 2004, for International Application No. PCT/US2004/023880.  |

\* Not enclosed, available upon request

|  |                 |
|--|-----------------|
| Examiner Signature   | Date Considered |
| EXAMINER: Initials citation considered. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. |                 |